

In the Claims

Please amend the claims as follows.

1. (Currently amended) A method for assessing therapeutic effectiveness of a treatment agent for renal disease and/or renal complications of a disease or condition, comprising:

- (a) administering a treatment agent to a patient;
- (b) obtaining a plurality of urine samples from the patient over time;
- (c) assaying for a protein in the urine samples by detecting either:
  - (1) ~~a native form of the protein and an intact modified form of the protein,~~

or

- (2) ~~an intact modified form of the protein; and~~

wherein(d) correlating a decreasing amount of the intact modified form of the protein over time in the urine ~~correlates~~ with effectiveness of the treatment agent.

2. (Currently amended) The method according to claim 1, wherein the renal disease and/or renal complications of the disease or condition is selected from the group consisting of nephropathy, diabetes insipidus, diabetes type I, diabetes type II, renal disease, glomerulonephritis, bacterial glomerulonephritis, viral glomerulonephritis, IgA nephropathy, Henoch-Schönlein Purpura, membranoproliferative glomerulonephritis, membranous nephropathy, Sjögren's syndrome, nephrotic syndrome, minimal change disease, focal glomerulosclerosis, acute renal failure, acute tubulointerstitial nephritis, pyelonephritis, GU tract inflammatory disease, Pre-clampsia, renal graft rejection, leprosy, reflux nephropathy, ~~nephrolithiasis)-~~ nephrolithiasis, genetic renal disease, medullary cystic disease, medullar

sponge, polycystic kidney disease, autosomal dominant polycystic kidney disease, autosomal recessive polycystic kidney disease, tuborous sclerosis, von Hippel-Lindau disease, familial thin-glomerular basement membrane disease, collagen III glomerulopathy, fibronectin glomerulopathy, Alport's syndrome, Fabry's disease, Nail-Patella Syndrome, congenital urologic anomalies, monoclonal gammopathies, multiple myeloma, amyloidosis, febrile illness, familial Mediterranean fever, HIV infection, ~~AIDS~~, AIDS, inflammatory disease, systemic vasculitides, polyarteritis nodosa, Wegener's granulomatosis, polyarteritis, necrotizing, crescentic glomerulonephritis, polymyositis-dermatomyositis, pancreatitis, rheumatoid arthritis, systemic lupus erythematosus, gout, blood disorders, sickle cell disease, thrombotic thrombocytopenia purpura, hemolytic-uremic syndrome, acute cortical necrosis, renal thromboembolism, trauma, side effect of surgery, extensive injury, burns, abdominal and vascular surgery, induction of anesthesia, side effect of use of drugs, drug abuse, malignant disease, adenocarcinoma, melanoma, lymphoreticular disease, multiple myeloma, circulatory disease, myocardial infarction, cardiac failure, peripheral vascular disease, hypertension, coronary heart disease, non-atherosclerotic cardiovascular disease, atherosclerotic cardiovascular disease, skin disease, psoriasis, systemic sclerosis, respiratory disease, chronic obstructive pulmonary disease (COPD), obstructive sleep apnoea, hypoxia at high altitude, endocrine disease, acromegaly, diabetes mellitus, and diabetes insipidus.

3. (Original) The method according to claim 1, wherein the treatment agent is a lysosome-activating compound.

4. (Original) The method according to claim 3, wherein the lysosome-activating compound is selected from the group consisting of ACE inhibitors, anti-glycation agents, anticancer compounds, antiproliferation compounds, and compounds that neutralize TGF-beta.

5. (Previously presented) The method according to claim 3, wherein the lysosome-activating compound is selected from the group consisting of ramipril, aminoguanidine, paracetamol, vitamin A, retinoic acid, retinol derivatives, and anti-TGF beta antibodies.

Claim 6. (Cancelled)

7. (Previously presented) The method of claim 1, wherein the protein is selected from the group consisting of albumin, globulin, alpha-globulin, alpha<sub>1</sub>-globulin, alpha<sub>2</sub>-globulin, beta-globulins, gamma-globulin, euglobulin, pseudoglobulin I and II, fibrinogen, alpha<sub>1</sub> acid glycoprotein (orosomucoid), alpha<sub>1</sub> glycoprotein, alpha<sub>1</sub> lipoprotein, ceruloplasmin, alpha<sub>2</sub> 19S glycoprotein, beta<sub>1</sub> transferring, beta<sub>1</sub> lipoprotein, immunoglobulins A, E, G and M, horseradish peroxidase, lactate dehydrogenase, glucose oxidase, myoglobin, lysozyme, protein hormone, growth hormone, insulin and parathyroid hormone.

8. (Cancelled).

9. (Previously presented) The method according to claim 8, wherein the assaying comprises:

(a) an antibody method, and

(b) a non-antibody method comprising chromatography, electrophoresis or sedimentation of the sample to test for the presence of the native form and the intact modified form of albumin.

10. (Previously presented) The method of claim 9, wherein the albumin is detected by an antibody or antibodies that recognizes and binds to both the native and intact modified forms of albumin, but does not bind to other peptides or polypeptides.

11. (Previously presented) The method according to claim 9, wherein the albumin is detected by an antibody that is specific for the intact modified albumin.

12. (Previously presented) The method according to claim 9, wherein the native albumin and/or intact, modified albumin is detected by an antibody that is attached to an enzymatic, radioactive, fluorescent or chemiluminescent label, wherein the detecting step comprises radioimmunoassay, immunoradiometric assay, fluorescent immunoassay, enzyme linked immunoassay, or protein A immunoassay.

13. (Currently amended) The method according to claim 1, wherein the assaying for a protein in the sample comprises the steps of;

- (i) detecting the native protein amount by conventional antibody assay; and
- (ii) detecting the native plus intact modified protein by a non-antibody method.

14. (Previously presented) The method according to claim 13, wherein the non-antibody method comprises chromatography, electrophoresis or sedimentation of the sample to test for native and intact modified protein.

Claim 15. (Cancelled)

16. (Previously presented) The method according to claim 1, wherein the assaying for a protein in the sample is by a method selected from the group consisting of partition chromatography, adsorption chromatography, paper chromatography, thin-layer chromatography, gas-liquid chromatography, gel chromatography, ion-exchange chromatography, affinity chromatography, hydrophobic interaction chromatography, moving boundary electrophoresis, zone electrophoresis, and isoelectric focusing.

17. (Original) The method according to claim 1, wherein the assaying for a protein in the sample is by hydrophobic interaction chromatography carried out in a high pressure liquid chromatography (HPLC) apparatus.

Claim 18. (Cancelled)

Claim 19 (Cancelled)

20. (Currently Amended). A method for identifying a treatment agent for renal disease and/or renal complications of a disease or condition comprising:

- (a) administering a candidate therapeutic agent to a patient;
- (b) obtaining a series of urine samples from the patient over time; and
- (c) assaying for a protein in each of the samples in the series of samples by detecting and determining total amount of either
  - (1) ~~a native form of the protein and an intact modified form of the protein, or~~
  - (2) an intact modified form of the protein,

wherein a decreasing amount of the intact modified form of the protein over time in the urine indicates that the candidate therapeutic agent is a treatment agent for the renal disease and/or the renal complications of a disease or condition.

Claim 21. (Cancelled)

22. (Previously presented). The method according to claim 13 wherein the protein is albumin.

23. (Currently Amended) The method of claim 20 wherein an antibody assay is used ~~in step (e)~~ to detect the intact modified form of the protein.

Claim 24. (Canceled)

25. (New) A method for assessing therapeutic effectiveness of a treatment agent for renal disease and/or renal complications of a disease or condition, comprising:

- (a) administering a treatment agent to a patient;
- (b) obtaining a plurality of urine samples from the patient over time;
- (c) assaying for a protein in the urine samples by detecting
  - 1) immunoreactive and immuno-nonreactive forms of the protein or
  - 2) immuno-nonreactive forms of the protein; and
- (d) correlating a decreasing amount of the immunoreactive and immuno-nonreactive forms of the protein or immuno-nonreactive forms of the protein over time in the urine with effectiveness of the treatment agent.

26. (New) The method of claim 25 wherein the immuno-nonreactive forms of the protein are detected with an antibody specific to the immuno-non-reactive form of the protein.